REMARKS

Objection of claims

According to the Office claims 2-9, 11 and 100 define properties that are inherent properties. Applicants disagree. Depending on the specific components and amounts thereof within the modifying moiety, the end products will exhibits different levels of activity. Clearly if the modifying moiety has a PAG moiety wherein "n" is 2 and an alkyl group with 20 carbons then it is likely to be more lipophilic. In the reverse, that being, a short alkyl chain and a long PEG chain, the conjugated group would likely be more hydrophilic. Thus, depending on the modifying moiety, the conjugate can exhibit different properties from that of the unconjugated compound. Applicants should be able to claim their invention according to their understanding of the invention and certainly functional language is acceptable to further define a result of the modifying moiety. Applicants request reconsideration of this objection.

Rejection of Claims and Traversal Thereof

In the February 4, 2009 Office Action:

1. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 §U.S.C. 112, second paragraph;

2. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §102(a) as being anticipated by US 2003/0069170;

3. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §102(a) as being anticipated by US 2003/0083232;

4. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §102(e) as being anticipated by US 6,770,625;

5. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §102(e) as being anticipated by US 6,867,183;

6. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §102(e) as being anticipated by US 7,030,082;

7. claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §103(a) as being obvious over US 7,030,082 or US 6,770,625 or US 2003/0069170;

8. claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 7-9, 11, 13, 41-50, 102, 105-110, 112-116, 118, 121, 122, 125, 128 and 129 of copending Application No. 10/999,761;

9. claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 7, 8, 10-58 of copending Application No. 11/138,194;

10. claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 14-25, 30, 31, 36-46, 51-67 of US Patent No 7,030,082; and

11. claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15, 19-36, 40-54, 58-76, 127-130 of US 6,770,625.

These rejections are traversed and reconsideration of the patentability of the pending claims is requested in light of the following remarks.

Rejection under 35 §U.S.C. 112, second paragraph

1. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 §U.S.C. 112, second paragraph for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants have amended claim 1 thereby obviating this rejection and request the withdrawal of same.

Rejections under 35 §U.S.C. 102(a)

2. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §102(a) as being anticipated by US 2003/0069170. Applicants submit that the US 2003/0069170 reference does not in any way disclose, teach or suggest the presently claimed invention.

It is well settled in the law that to constitute anticipation, a single prior art reference must disclose each and every material element of the claim. *In re* Marshall, 198, USPQ 344, 346 (CCPA 1978). US 2003/0069170 merely discloses a broad genus of formulations with thousands of permutations. When the claimed compound(s) are not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternative components to arrive at a specific composition, anticipation can only be found if the classes of different components are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). (MPEP 2131.03).

In the present matter, one skilled in the art reading US 2003/0069170 would have to pick one of the many optional drugs, determine that a bile salt is no longer required, choose amount thousands of possibilities of PEG containing structures, the number of PEG subunits, the length of alkyl groups, and numerous other optional choices.

Clearly, from the lists of different components set forth in US 2003/0069170, identifying an anticipatory formulation would certainly be a serendipitous event because US 2003/0069170 provides no guidance or suggestion to go in the direction of applicants' claimed invention. Certainly there is no anticipation when the disclosure in the reference is so broad that the likelihood of arriving at the claimed formulations would be the same as discovering the combination of a safe by an inspection of its dials, *Ex parte Garvey*, 41 USPQ 583 (POBA 1939).

Thus, applicants believe that the cited reference does not qualify as a reference under 35 U.S.C. §102.

3. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §102(a) as being anticipated by US 2003/0083232. Applicants submit that the US 2003/0069170 reference does not in any way disclose, teach or suggest the presently claimed invention. Applicants have amended claim 1 to recited that the biologically active natriuretic compound is a brain natriuretic peptide, atrial natriuretic peptide, C-type natriuretic peptide, dendroaspis natriuretic

peptide or a biologically active segment thereof. Clearly this reference does not disclose this claim limitation and as such is not anticipatory. Applicants request the withdrawal of same.

Rejection under 35 §U.S.C. 102(e)

4. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §102(e) as being anticipated by US 6,770,625. Applicants make the same argument as set for above for the 102(a) rejection for the publish application corresponding to this issued patent. It is well settled in the law that to constitute anticipation, a single prior art reference must disclose each and every material element of the claim. *In re* Marshall, 198, USPQ 344, 346 (CCPA 1978). US 6,770,625 merely discloses a broad genus of formulations with thousands of permutations. When the claimed compound(s) are not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternative components to arrive at a specific composition, anticipation can only be found if the classes of different components are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). (MPEP 2131.03).

In the present matter, one skilled in the art reading US 6,770,625 would have to pick one of the many optional drugs, determine that a bile salt is no longer required, choose amount thousands of possibilities of PEG containing structures, the number of PEG subunits, the length of alkyl groups, and numerous other optional choices.

Clearly, from the lists of different components set forth in US 6,770,625, identifying an anticipatory formulation would certainly be a serendipitous event because US 6,770,625 provides no guidance or suggestion to go in the direction of applicants' claimed invention. Certainly there is no anticipation when the disclosure in the reference is so broad that the likelihood of arriving at the claimed formulations would be the same as discovering the combination of a safe by an inspection of its dials, *Ex parte Garvey*, 41 USPQ 583 (POBA 1939). Thus, applicants believe that the cited reference does not qualify as a reference under 35 U.S.C. §102 and request the withdrawal of this rejection for anticipation.

5. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §102(e) as being anticipated by US 6,867,183. Applicants submit that the US 6,867,183 reference does not in any way disclose, teach or suggest the presently claimed invention. Applicants have amended claim 1 to recited that the biologically active natriuretic compound

is a brain natriuretic peptide, atrial natriuretic peptide, C-type natriuretic peptide, dendroaspis natriuretic peptide or a biologically active segment thereof. Clearly this reference does not disclose this claim limitation and as such is not anticipatory. Applicants request the withdrawal of same.

6. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §102(e) as being anticipated by US 7,030,082. This patent is a CIP of US 6,770,625 and suffers from exactly the same shortcomings.

It is well settled in the law that to constitute anticipation, a single prior art reference must disclose each and every material element of the claim. *In re* Marshall, 198, USPQ 344, 346 (CCPA 1978). US 7,030,082 merely discloses a broad genus of formulations with thousands of permutations. When the claimed compound(s) are not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternative components to arrive at a specific composition, anticipation can only be found if the classes of different components are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). (MPEP 2131.03).

In the present matter, one skilled in the art reading US 7,030,082 would have to pick one of the many optional drugs, determine that a bile salt is no longer required, choose amount thousands of possibilities of PEG containing structures, the number of PEG subunits, the length of alkyl groups, and numerous other optional choices.

Clearly, from the lists of different components set forth in US 7,030,082, identifying an anticipatory formulation would certainly be a serendipitous event because US 7,030,082 provides no guidance or suggestion to go in the direction of applicants' claimed invention. Certainly there is no anticipation when the disclosure in the reference is so broad that the likelihood of arriving at the claimed formulations would be the same as discovering the combination of a safe by an inspection of its dials, *Ex parte Garvey*, 41 USPQ 583 (POBA 1939). Thus, applicants believe that the cited reference does not qualify as a reference under 35 U.S.C. §102 and request the withdrawal of this rejection for anticipation.

Rejections under 35 U.S.C. §103(a)

7. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected under 35 U.S.C. §103(a) as being obvious over US 7,030,082 or US 6,770,625 or US

2003/0069170. Applicants hereby declare and affirm that U.S. Patent Nos. 7,030,082 and US 6,770,625 in the name of Soltera, et al, and assigned to Nobex Corporation were at the time of filing the present invention on November 30, 2004 also owned by Nobex Corporation. As such, these rejections for obviousness should be withdrawn.

US 2003/0069170, the published application of US Patent No. 6,770,625, has also been cited as rendering the presently claimed invention as obvious. Applicants insists that the thousands of different possibilities as set forth in this cited application provides no guidance for applicants to go in the direction of applicants' claimed invention. As previously stated, the *Kubin* Court ruled on this very matter and stated that:

> what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.

Clearly, this is relevant to the present situation and as described in US Publication No. 2003/0069170, wherein thousands of drugs are cited in addition to thousands of possible permutations for the PEG molecules. One skilled in the art would have to try thousands of different combinations in the hope of tripping upon the presently claimed invention.

Further, this concept of an infinite number of choices has been addressed by the Federal Circuit in the *Takeda* ruling. Specifically, the Court in *Takeda Chemical Industries Ltd. v. Alphapharm Ltd.*, 83 USPQ2d 1169 (Fed. Cir 2007) determined that the cited prior art disclosed thousands of possible compounds, including the compound(s) that the infringer contended were invalid. Notably, even though the nine compounds were exactly defined in the prior art, meaning the compound with all specific substituents were described, the *Takeda* Court ruled that nothing in the prior art suggested to one skilled in the art that those nine compounds, out of thousands of compounds covered by the patent of the prior art, provided any indication that the compounds were of value. Thus, even if the prior art reference provides a broad selection of compounds but provides no guidance regarding which of the many compounds will be effective for a specific purpose or which structure is important for that specific purpose, then it would not fall into the situation contemplated by the *KSR* Court as an "obvious to try" invention. Again the present situation fits this fact pattern.

As stated by the Court in *In re Kratz*, 201 U.S.P.Q. 71 (C.C.P.A. 1979), "[e]ven if the bare lists of components found ...were in the prior art, those extensive lists are quite mute in directing one having ordinary skill in the art to any particular compound for any purpose." The Court reversed the Examiner's rejection for obviousness, and stated that for there to be a denial of patentability "the prior art itself [should] further provide some foreseeability or predictability that the compound is a significant...ingredient." Further, the fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious. *In re Jones* 21 USPQ2d 1941, (Fed. Cir. 1992). *Jones* involved an obviousness rejection of a claim to specific compounds wherein a prior art reference disclosed a genus, which encompassed some of the claimed compounds. However, the *Jones* Court found that the prior art reference encompassed a "potentially infinite genus" but did not disclose or suggest the claimed compounds. As such, the rejection by the examiner for obviousness was reversed.

Applicants request the withdrawal of this rejection for obviousness.

Rejections under Judicially Created Doctrine of Obviousness-type Double Patenting

8. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 7-9, 11, 13, 41-50, 102, 105-110, 112-116, 118, 121, 122, 125, 128 and 129 of copending Application No. 10/999,761. A review of the Image File Wrapper for co-pending U.S. Patent Application 10/999,761 shows that the claims of these applications are still in the prosecution stage and until patentable claims are determined, applicants submit that there is no clear idea of whether the claims will render the current claims in this application as obvious. As such, applicants will delay filing such terminal disclaimers until it is determined that one is absolutely necessary.

9. claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 7, 8, 10-58 of copending Application No. 11/138,194. A review of the Image File Wrapper for co-pending U.S. Patent Application 11/134,194 shows that the claims of these applications are still in the prosecution stage and until patentable claims are determined, applicants submit that there is no clear idea of whether the claims will render the current claims in this application as obvious. As such, applicants will delay filing such terminal disclaimers until it is determined that one is absolutely necessary.

10. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 14-25, 30, 31, 36-46, 51-67 of US Patent No 7,030,082.

The Office fails to see any patentable differences between the subject matter of the current pending claims of the subject application and the subject matter encompassed by claims 1-10, 14-25, 30, 31, 36-46, 51-67 of US Patent No 7,030,082. Applicants submit that the claims of US Patent No 7,030,082 differ greatly from the present claims because all the independent claims of US Patent No 7,030,082 must include a bile salt as shown below in claim 1.

The invention claimed is:

1. A pharmaceutical composition comprising (a) a drug-oligomer conjugate comprising a drug covalently coupled to an oligomeric moiety, wherein the oligomeric moiety is hydrophilic, (b) a bile salt, and (c) a pharmaceutically acceptable carrier.

In contrast, the presently claimed invention does not include a bile salt. Notably, there is no teaching or suggestion in the claims of the US Patent No 7,030,082 patent that the composition does not include the bile salt. As stated above, the Office is not at liberty to resort to the text of the US Patent No 7,030,082 patent for the obviousness-type double patenting rejection. In all instances, only the literal language of the claims of the US Patent No 7,030,082 patent may be considered in arriving at the conclusion of obviousness-type double patenting. Because the Office has not provided the Applicants with any factual basis and/or rationale to support the conclusion that the presently claimed invention is an obvious variation of the previously issued patent, the double patenting rejection of the present claims cannot stand. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

11. Claims 1-9, 11, 28, 29, 40-42, 86, 89-94, 96-98, 100, 101, 103, 105, 106, 109, 112, 113 and 156-159 were rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15, 19-36, 40-54, 58-76, 127-130 of US 6,770,625.

This rejection suffers from the same shortcomings as that of US Patent No. 7,030,082. The Office fails to see any patentable differences between the subject matter of the current pending claims of the subject application and the subject matter encompassed by claims 1-15, 19-36, 40-54, 58-76, 127-130 of US 6,770,625. Applicants submit that the claims of US 6,770,625 differ greatly from the present claims because all the independent claims of US 6,770,625 must include a bile salt as shown below in claim 1.

1. A pharmaceutical composition comprising:
a drug-oligomer conjugate comprising a drug covalently coupled to an oligomeric moiety and wherein the drug is a calcitonin polypeptide;
a fatty acid component comprising a fatty acid; and
a bile salt component comprising a bile salt; wherein the fatty acid component and the bile salt component are present in a weight-to-weight ratio of between 1:5 and 5:1, wherein the fatty acid component is present in an amount sufficient to lower the precipitation point of the bile salt compared to a precipitation point of the bile salt if the fatty acid component were not present in the pharmaceutical composition, and wherein the bile salt component is present in an amount sufficient to lower the solubility point of the fatty acid compared to a solubility point of the fatty acid if the bile salt were not present in the pharmaceutical composition.

In contrast, the presently claimed invention does not include a bile salt. Notably, there is no teaching or suggestion in the claims of the US 6,770,625 patent that the composition does not include the bile salt. As stated above, the Office is not at liberty to resort to the text of the US 6,770,625 patent for the obviousness-type double patenting rejection. In all instances, only the literal language of the claims of the US 6,770,625 patent may be considered in arriving at the conclusion of obviousness-type double patenting. Because the Office has not provided the Applicants with any factual basis and/or rationale to support the conclusion that the presently claimed invention is an obvious variation of the previously issued patent, the double patenting rejection of the present claims cannot stand. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejoinder of method claims

Applicants request that method claims depending from claim 1 be rejoined. Specifically, applicants request the rejoining of method of treatment claims 114 to 121 and method of making claims 122-126 and 173 to 175.

Petition for Extension of Time/Fees Payable

The applicants hereby petition for a one month extension of time, extending the deadline from May 4, to June 4, 2009. The entry of this petition results in a petition fee of $130.00. The petition fee in being submitted by electronic transfer along with the electronic filing of this response. In the event an additional fee is found due, the U.S. Patent and Trademark Office is hereby authorized to charge any

additional amount necessary to the entry of this amendment to Deposit Account No. 13-4365 of Moore & Van Allen PLLC.

Conclusion

Applicants have satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Kosar reconsider the patentability of pending claims in light of the distinguishing remarks herein and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Kosar is requested to contact the undersigned attorney at (919) 286-8089 to resolve same.

Respectfully submitted,

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